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L8: Entry 5 of 5 File: USPT Mar 29, 1994

DOCUMENT-IDENTIFIER: US 5297562 A
TITLE: Method for detecting and treating Alzheimer's disease

US Patent No. (1):
5297562

Detailed Description Text (27):
Because the data indicate that Alzheimer's disease is a mosaic form of Down syndrome, due to nondisjunction (but perhaps during meiosis followed by nondisjunction early in development to yield normal cells), much Alzheimer's disease may be prevented by preventing the nondisjunction from occurring, including such approaches as avoiding environmental agents that cause translocation by inducing chromosome nondisjunction, treatment with agents that reduce spontaneous nondisjunction or that obviate the effects of environmental agents, and mitotic inhibitors such as colcemid or methyl benzimidazole-2-yl-carbamate. Such treatment might include, but is not limited to, heavy metal chelaters, antoxidants, and promoters of microtubule assembly. Drugs that improve chromosome segregation will include those that affect DNA toposiomerase II (Holm et al., Mol. Cel. Biol. 9:159 (1989)), or centromere binding proteins such as CBF1 (Cai and Davis, Nature 349:704 (1991)), or DYS1 (Rockmill and Fogel, Genetics 119:261 (1988)). An additional approach may be to treat patients with drugs to which trisomy 21 cells may be particularly sensitive in the expectation that they will be preferentially killed and thus no longer pose a threat to the patient. This may be accomplished by killing cells that have an excess of certain cell surface markers known to be increased in cells from Down syndrome patients due to the trisomy 21. These include the cell surface marker S14 and interferon-.alpha. receptor.

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L15: Entry 3 of 3 File: USPT Jul 1, 1997

DOCUMENT-IDENTIFIER: US 5643749 A
TITLE: Soluble interferon .alpha.-receptor, its preparation and use

US Patent No. (1):
5643749

Brief Summary Text (20):
Moreover, the present invention also provides a pharmaceutical composition formulated from the above composition of the invention and a pharmaceutically acceptable diluent, carrier and/or excipient; the pharmaceutical composition being for the modulation, inhibition or modification of the activities of IFN-.alpha. and IFN-.beta. subtypes in cells and/or tissues; or for the treatment of patients having excess amounts of IFNs as a result of IFN treatment or excess endogenous IFN production.

Detailed Description Text (4):
Applications of the novel, soluble IFNAR forms of the present invention could be for inhibiting, modulating or modifying the activities of IFN-.alpha. and IFN-.beta. subtypes in cells, tissues and organisms. IFNs have antiviral, anti-proliferative and immunoregulatory functions (Baron, S. et al.(eds), Interferon: Principles and Medical Applications, The University of Texas Medical Branch at Galveston, (1992)). IFNs are used clinically to treat viral diseases (e.g. papillomatoses, hepatitis, etc.) malignancies (e.g. leukemias, hormone-dependent cancers, etc.) and immunological dysfunctions (e.g. multiple sclerosis). These beneficial effects of IFNs may be naturally modulated by the different forms of the IFN m-receptor such as those of the present invention. On the other hand, excess of IFN may be detrimental and has been implicated in some auto-immune diseases, in graft rejections and hematopoietic deficiences (locus cited). These conditions may benefit from inhibitors of IFN action. Furthermore, cells can differ in their response to IFN-.alpha. and IFN-.beta. subtypes (Rosenblum, M. G. et al., J. Interferon Res. 10,141-151 (1990)), and the cell response to IFN subtypes may be modulated by some of the cell-synthesized soluble IFNAR forms. The isolation and identification of novel IFNAR cDNAs according to the present invention, will allow the production of the natural cell-synthesized soluble IFN .alpha.-receptor forms by recombinant DNA technology and the study of their functions by overexpression in transfected cells, or by addition to cell cultures.

Detailed Description Text (5):
The soluble IFNAR forms according to the present invention may be used to prepare pharmaceutical compositions for inhibiting, modulating or modifying the activities of IFN-.alpha. and IFN-.beta. subtypes. Such pharmaceutical compositions may be used, for example, for the treatment of various disorders, as noted above, in which patients have an excess of IFNs as a result of receiving large doses of IFN in therapy or as a result of abnormally high endogenous production of IFNs. The pharmaceutical compositions may be prepared by any of the well known procedures in which the active ingredient, soluble IFNAR, is admixed with pharmaceutically acceptable diluents, carriers or excipients. Actual dosages and modes of administration of such pharmaceutical compositions will be determined by the professional practitioners.

Detailed Description Text (63):
An isolated cDNA according to the invention is subjected to site directed mutagenesis with appropriate oligo-nucleotides so that a termination codon and a polyadenylation site are inserted after the last essential codon of the soluble IFNAR. This construct is then inserted into appropriately constructed expression vectors by techniques well known in the art (Maniatis et al. Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory, New York, 1982). Double-stranded cDNA is linked to plasmid vectors

by homopolymeric tailing or by restriction linking involving the use of synthetic DNA linkers or blunt-ended ligation techniques. DNA ligases are used to ligate the DNA molecules and undesirable joining is avoided by treatment of DNA strands with alkaline phosphatase.

Detailed Description Text (71):
Preferred eukaryotic plasmids include BPV, vaccinia, SV40, 2-micron circle, etc., or their derivatives. Suck plasmids are well known in the art (Botstein, D., et al. (1982) Miami Wint. Symp. 19:265-274; Broach, J. R., in "The Molecular Biology of the Yeast Saccharomyces: Life Cycle and Inheritance", Cold Spring Harbor Laboratory, Cold Spring Harbor, N.Y., pp. 445-470 (1981); Broach, J. R., (1982) Cell 28:203-204; Bollon, D. P., et al. 1980) J. Clin. Hematol. Oncol. 10:39-48; Maniatis, T., in "Cell Biology: A Comprehensive Treatise, Vol. 3: Gene Expression", Academic Press, New York, pp. 563-608 (1980)).

L12 ANSWER 16 OF 19 MEDLINE
AN 91249841 MEDLINE
DN 91249841 PubMed ID: 1828230
TI Purification and biochemical characterization of a **soluble** mouse **interferon**-gamma **receptor** produced in insect cells.
AU Fountoulakis M; Schlaeger E J; Gentz R; Juranville J F; Manneberg M; Ozmen L; Garotta G
CS Hoffmann-La Roche Ltd, Central Research Unit, Basel, Switzerland.
SO EUROPEAN JOURNAL OF BIOCHEMISTRY, **(1991 Jun 1)** 198 (2) 441-50.
Journal code: 0107600. ISSN: 0014-2956.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199107
ED Entered STN: 19910728
Last Updated on STN: 19970203
Entered Medline: 19910710
AB The extracellular domain of the mouse interferon gamma receptor comprising amino acids 17-243 of the protein was produced in Spodoptera frugiperda cells infected with a recombinant baculovirus. The receptor was mainly secreted into the culture medium and was purified to homogeneity in several hundred milligram amounts. The purification procedure involved four chromatography steps and delivered a soluble and active receptor with an overall recovery of 30%. From each purification run, two pools of **soluble receptor** with the same **interferon** gamma binding capacity were isolated. Under reducing electrophoretic conditions the protein of pool I migrates as two bands of molecular masses 32 and 34 kDa and of pool II as two bands of 30 and 32 kDa. The soluble receptor of both pools carries a heterogeneous glycosylation. After deglycosylation it appears as one protein band of 27 kDa. N-linked carbohydrates contribute about 6 kDa and O-linked carbohydrates 1 kDa to its molecular mass. The nonreduced protein specifically binds interferon gamma on ligand blots and in a solid-phase binding system and competes for the binding of radiolabeled interferon gamma to the cell surface receptor. The **soluble** mouse **interferon** gamma **receptor** exists as a monomer in physiological buffer and binds interferon gamma in its dimeric form. It is stable at room temperature and against tryptic digestion, but is very sensitive to proteinase K digestion. The **soluble** mouse **interferon** gamma **receptor** produced in the insect/baculovirus expression system may prove useful to study the function of interferon gamma receptor as an antagonist of endogenous interferon gamma in the **treatment** of immunological and inflammatory disorders.

Soluble interferon antagonist

Journal code: 0220042. ISSN: 0003-4762.
CY Finland
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198901
ED Entered STN: 19900308
Last Updated on STN: 19970203
Entered Medline: 19890105
AB An elderly man with small cell lung cancer developed a largely reversible, **dementia**-like syndrome after cranial irradiation and prolonged **treatment** with **interferon** (IFN). The development of the symptoms started 2 months after cranial irradiation following more than 2 years of IFN **treatment**. The behavioral impairment did not suggest any specific brain localization. The **dementia**-like behaviour may be due to a combined effect of irradiation and IFN.

ED Entered STN: 19920904
Last Updated on STN: 20000303
Entered Medline: 19920817

AB A cohort of 35 patients with advanced colorectal cancer, not previously exposed to chemotherapy, were included in a phase II study exploring the combination of **interferon**-alpha, 9 MU subcutaneously three times weekly, and 5-fluorouracil 750 mg/m2/day during 5 consecutive days in continuous intravenous infusion followed with weekly bolus injection of fluorouracil 750 mg/m2. Of 33 cases evaluable for activity; 5 patients achieved partial response and 3 complete response for an overall response rate of 24% (95%; confidence limit 11-42%). Most of the responses were observed in liver metastases, response rate = 30% (95%; CL 13-53%), with little activity observed in other sites; response rate 3% (95%; CL 8-16%), p = .0006. The median time to progression and median overall survival were 16+ (range 1+ to 48+) and 21+ weeks (range 1+ to 52+). All patients were evaluable for analysis of toxicity. Severe mucositis and diarrhea, present in 14 patients were the limiting side effects. Two patients developed progressive renal toxicity and died. Weakness, myalgia, and nonneutropenic fever were observed frequently, one patient developed **dementia**. This combination is able to induce major responses in patients with advanced colorectal cancer, particularly in liver metastasis. Additional trials evaluating this approach are indicated.

L9 ANSWER 6 OF 14 MEDLINE
AN 92213476 MEDLINE
DN 92213476 PubMed ID: 1557642
TI Alfa-2A **interferon** and 5-fluorouracil for advanced colorectal carcinoma: the Memorial Sloan-Kettering experience.
AU Kemeny N; Younes A
CS Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York, NY 10021.
SO SEMINARS IN ONCOLOGY, **(1992 Apr)** 19 (2 Suppl 3) 171-5.
Journal code: 0420432. ISSN: 0093-7754.
CY United States
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199205
ED Entered STN: 19920515
Last Updated on STN: 19920515
Entered Medline: 19920501

AB In a phase II study, 38 previously untreated patients with metastatic colorectal carcinoma were **treated** with continuous intravenous infusion of 5-fluorouracil (5-FU) 750 mg/m2 daily for 5 days, followed by weekly bolus 5-FU at 750 mg/m2 and subcutaneous **interferon** (IFN) at 9 million units three times per week. Of 35 evaluable patients, nine (26%) achieved a partial response (95% confidence limit, 11% to 41%), with a median response duration of 7.5 months (range, 4.4 to 17+ months). Seven patients (20%) had a minor response, and 10 (28%) had stable disease. The median length of survival was 13 months (range, 2 to 19+ months). The most common toxicities observed were stomatitis (52%) and diarrhea (43%). Neurotoxicity was seen in 34% of patients and consisted of gait disturbance, dizziness, confusion, memory loss, and **dementia**. Because of toxicity, 84% of patients required a reduction of the IFN dose by at least 50%, and 63% required reduction of 5-FU by at least 25%. We conclude that while the combination of 5-FU and IFN in patients with advanced colorectal carcinoma has some activity, the regimen is toxic and the observed response rate (26%) is not substantially superior to alternative 5-FU programs.

L9 ANSWER 7 OF 14 MEDLINE.

AN 92081110 MEDLINE
DN 92081110 PubMed ID: 1746062
TI **Interferon**-related leukoencephalopathy in a patient with renal cell carcinoma.
AU Merimsky O; Reider I; Merimsky E; Chaitchik S
CS Department of Oncology, Tel-Aviv Sourasky Medical Center, Tel-Aviv University, Israel.
SO TUMORI, **(1991 Aug 31)** 77 (4) 361-2.
Journal code: 0111356. ISSN: 0300-8916.
CY Italy
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199201
ED Entered STN: 19920202
Last Updated on STN: 20000303
Entered Medline: 19920110
AB A 75-year-old patient with metastatic renal cell carcinoma was **treated** with recombinant **interferon** alpha-C and thereafter developed a neurologic syndrome of **dementia**, ataxia, confusional state, loss of concentration ability and cortical blindness. CT scan findings were compatible with leukoencephalopathy, which is reported as being a toxic effect of **interferon**.

L9 ANSWER 8 OF 14 MEDLINE
AN 91278769 MEDLINE
DN 91278769 PubMed ID: 2056927
TI The immune system is a key factor in the etiology of psychosocial disease.
AU Smith R S
SO MEDICAL HYPOTHESES, **(1991 Jan)** 34 (1) 49-57. Ref: 69
Journal code: 7505668. ISSN: 0306-9877.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals; AIDS
EM 199107
ED Entered STN: 19910818
Last Updated on STN: 19970203
Entered Medline: 19910729
AB The immune system is proposed as the key to understanding the etiology and **treatment** of psychosocial disease. There is a dense communication network between the immune system and the central nervous system (CNS). Immune cell cytokines, via direct action on the CNS, induce fever, alter sleep, pain perception and pituitary hormone release and reduce appetite and activity in animals. Interleukin-2 and **interferon** given to humans result in global behavioral and cognitive pathology. Activation of the immune system by pathogens produces global cognitive and behavioral pathology also. Recently, controlled trials have demonstrated that diet can cause psychosocial disease, presumably by an immune mechanism. Immune system abnormalities have been identified in manic-depressive psychosis, schizophrenia and alcoholism. Lithium carbonate is not only prophylactic for all three of these diseases, but it also powerfully stimulates the immune system. This is proposed as the mechanism of lithium's therapeutic effect. The antipsychotics, haloperidol and the phenothiazines, affect the immune system also. The rapid development of AIDS **dementia** complex can be explained by the remarkable influence the immune system has on the CNS.

L9 ANSWER 9 OF 14 MEDLINE
AN 91064679 MEDLINE

DN 91064679 PubMed ID: 2249187
TI **Interferon** alpha-2a and 5-fluorouracil for advanced colorectal carcinoma. Assessment of activity and toxicity.
AU Kemeny N; Younes A; Seiter K; Kelsen D; Sammarco P; Adams L; Derby S; Murray P; Houston C
CS Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York, New York 10021.
SO CANCER, **(1990 Dec 15)** 66 (12) 2470-5.
Journal code: 0374236. ISSN: 0008-543X.
CY United States
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199101
ED Entered STN: 19910308
Last Updated on STN: 19910308
Entered Medline: 19910117
AB Preclinical data showed that the cytotoxic effects of 5-fluorouracil (5-FU) are augmented by **interferon** (IFN). In a small study, 13 of 17 patients with advanced colorectal cancer responded to a regimen of 5-FU with IFN. Using the same dose and schedule as in this pilot study, 38 previously untreated patients with metastatic colorectal carcinoma were **treated** with continuous intravenous (IV) infusion of 5-FU 750 mg/m2 daily for 5 days, followed by weekly bolus 5-FU at 750 mg/m2 and subcutaneous IFN at 9 million units three times per week. Of 35 evaluable patients, nine (26%) had a partial response (95% confidence limit, 11% to 41%), with a median response duration of 7.5 months (range, 4.4 to greater than 11.7 months). Seven patients (20%) had a minor response, and ten (28%) had stable disease. The most common toxicities observed were stomatitis (52%) and diarrhea (43%). Neurotoxicity was seen in 34% of patients and consisted of gait disturbance, dizziness, confusion, memory loss, and **dementia**. Because of toxicity, 84% of patients required a reduction of the IFN dose by at least 50%, and 63% required reduction of the 5-FU dose by at least 25%. Although the combination of 5-FU and IFN in patients with advanced colorectal carcinoma has some activity, the regimen was toxic, and the observed response rate (26%) was not substantially superior to alternative 5-FU programs.

L9 ANSWER 10 OF 14 MEDLINE
AN 90380472 MEDLINE
DN 90380472 PubMed ID: 2144747
TI **Interferon**-related mental deterioration and behavioral changes in patients with renal cell carcinoma.
AU Merimsky O; Reider-Groswasser I; Inbar M; Chaitchik S
CS Department of Oncology, Tel Aviv Sourasky Center, Ichilov Hospital, Israel.
SO EUROPEAN JOURNAL OF CANCER, **(1990)** 26 (5) 596-600.
Journal code: 9005373. ISSN: 0959-8049.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199010
ED Entered STN: 19901122
Last Updated on STN: 20000303
Entered Medline: 19901024
AB Five out of 38 patients (13%) with metastatic renal cell carcinoma had mental deterioration 3 weeks to 13 months after the start of **treatment** with recombinant **interferon** alpha-C.
Metastatic spread to the brain, paraneoplastic effect of the tumor on the central nervous system and other causes of **dementia** were

excluded. Computed tomography of the brain in these patients was normal and the width of the cerebral sulci and ventricles did not correlate with the severity of **dementia**. Specific patterns of atrophy were not seen. General deterioration, assessed by the change in Karnofsky performance status, was associated with **dementia**. The **dementia** may have been caused by a neurotoxic effect of **interferon**.

L9 ANSWER 11 OF 14 MEDLINE
AN 90359747 MEDLINE
DN 90359747 PubMed ID: 1697183
TI Early detection and diagnosis of neurobehavioral disorders associated with cancer and its **treatment**.
AU Meyers C A; Scheibel R S
CS Department of Neuro-Oncology, MD Anderson Cancer Center, Houston, Texas 77030.
SO ONCOLOGY, **(1990 Jul)** 4 (7) 115-22; discussion 122, 126-7, 130.
Journal code: 8712059. ISSN: 0890-9091.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199010
ED Entered STN: 19901109
Last Updated on STN: 19960129
Entered Medline: 19901002
AB The cognitive and behavioral disorders associated with cancer and its **treatments** can have a tremendous impact on patients' quality of life. Brain tumors, leptomeningeal disease, and paraneoplastic syndromes have all been shown to cause specific neurobehavioral abnormalities. In addition, cancer patients frequently develop cognitive and behavioral alterations during or after radiation therapy, chemotherapy, or immunotherapy. Although some impairments are acute and reversible, others may persist after the cessation of **treatment** or have a delayed onset. These neurobehavioral disorders can range from profound intellectual decline (**dementia**) to subtle deficits evident only on sensitive neuropsychological tests. Even mild cognitive impairments may compromise an individual's ability to return to work or other activities.

L9 ANSWER 12 OF 14 MEDLINE
AN 90105183 MEDLINE
DN 90105183 PubMed ID: 2557881
TI Recombinant alpha 2 **interferon** is superior to doxorubicin for inoperable hepatocellular carcinoma: a prospective randomised trial.
AU Lai C L; Wu P C; Lok A S; Lin H J; Ngan H; Lau J Y; Chung H T; Ng M M; Yeoh E K; Arnold M
CS Department of Medicine, University of Hong Kong, Queen Mary Hospital.
SO BRITISH JOURNAL OF CANCER, **(1989 Dec)** 60 (6) 928-33.
Journal code: 0370635. ISSN: 0007-0920.
CY ENGLAND: United Kingdom
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LA English
FS Priority Journals
EM 199002
ED Entered STN: 19900328
Last Updated on STN: 20000303
Entered Medline: 19900220
AB In a prospective trial of 75 Chinese patients with histologically proven inoperable hepatocellular carcinoma (HCC), 25 patients were randomised to

receive doxorubicin 60-75 mg m-2 intravenously once every 3 weeks, 25 to receive recombinant alpha 2 **interferon** (rIFN) (Roferon) 9-18 x 10(6) IU m-2 intramuscularly (i.m.) daily and 25 to receive rIFN 25-50 x 10(6) IU m-2 i.m. three times weekly. Patients were switched to the other drug if: (a) there was progressive disease after 12 weeks, (b) unacceptable toxicity developed and (c) they had received a total of 500 mg m-2 of doxorubicin. Six patients had switching over of therapy, three on doxorubicin and three on rIFN. In the remaining 69 patients on single drug therapy, the median survival rate of patients on doxorubicin and rIFN was 4.8 and 8.3 weeks respectively (P = ns.). rIFN induced tumour regression of 25-50% in 12% of patients and of over 50% in 10% of patients. When compared with doxorubicin, rIFN was associated with more tumour regression (P = 0.00199) and less progressive tumours (P = 0.00017). It caused less prolonged and less severe marrow suppression (P = 0.01217), and had significantly less fatal complications than doxorubicin (P = 0.01383). Doxorubicin caused fatal complications due to cardiotoxicity and neutropenia in 25% of patients. rIFN was associated with fatal complications due to **dementia** and renal failure in 3.8% of patients. In the **treatment** of inoperable HCC, rIFN is superior to doxorubicin in causing more tumour regression, less serious marrow suppression and less fatal complications.

L9 ANSWER 13 OF 14 MEDLINE
AN 89236665 MEDLINE
DN 89236665 PubMed ID: 2716192
TI The trial use of alpha-IFN in **treating** a case of chronic myelomonocytic leukemia with splenic infarction.
AU Kimura S; Yokoo K; Ozawa M; Kobayashi Y; Horiuchi H; Kondo M
CS 1st Dept. of Int. Med., Kyoto Prefectural Univ. of Med.
SO GAN NO RINSHO. JAPANESE JOURNAL OF CANCER CLINICS, **(1989 Apr)** 35 (5) 615-9.
Journal code: 1257753. ISSN: 0021-4949.
CY Japan
DT Journal; Article; (JOURNAL ARTICLE)
LA Japanese
FS Priority Journals
EM 198906
ED Entered STN: 19900306
Last Updated on STN: 19900306
Entered Medline: 19890615
AB A 75-year-old man, previously diagnosed as having chronic myelomonocytic leukemia, suffered an attack of severe left hypochondralgia in July 1986. A splenic infarction was diagnosed by both ultrasound tomography and computerized tomography. The patient was **treated** with alpha-**Interferon** (600 M.U./day i.m.) for cytoreduction in order to prevent a recurrence of the splenic infarction. Twenty-one days later, the peripheral white blood cell count decreased from 44,110 microliters to 9800/microliters and the monocytoid immature cells disappeared. However, severe **dementia** appeared and so alpha-**Interferon** therapy was abandoned. In this report the beneficial effects and side effects of alpha-**interferon** in the **treatment** of chronic myelomonocytic leukemia are discussed.

L9 ANSWER 14 OF 14 MEDLINE
AN 89060974 MEDLINE
DN 89060974 PubMed ID: 2848440
TI **Dementia**-like, largely reversible syndrome after cranial irradiation and prolonged **interferon treatment**.
AU Laaksonen R; Niiranen A; Iivanainen M; Mattson K; Holsti L; Farkkila M; Cantell K
CS Department of Neurology, University Central Hospital, Helsinki, Finland.
SO ANNALS OF CLINICAL RESEARCH, **(1988)** 20 (3) 201-3.

abnormalities including intracerebral arteriosclerosis and cerebral atrophy may increase susceptibility to unacceptably severe IFN neurotoxicity.

L9 ANSWER 4 OF 14 MEDLINE
AN 93029969 MEDLINE
DN 93029969 PubMed ID: 1329171
TI [Value of **interferon** alpha determination in the diagnosis of meningoencephalitis presumed to be of viral origin].
Interet du dosage de l'**interferon** alpha dans le diagnostic des meningo-encephalites presumees virales.
AU Bocket L; Delforge F; Wattre P; Lemaitre J F; Hober D; Dewilde A
CS Service de Bacteriologie Virologie B, CHRU, Lille.
SO REVUE DE MEDECINE INTERNE, **(1992 Jan-Feb)** 13 (1) 27-31.
Journal code: 8101383. ISSN: 0248-8663.
CY France
DT Journal; Article; (JOURNAL ARTICLE)
LA French
FS Priority Journals
EM 199211
ED Entered STN: 19930122
Last Updated on STN: 19930122
Entered Medline: 19921125
AB Quantitative determination of alpha **interferon** (IFN) is used as an early marker in viral encephalitis. IFN is detected during 10 days following the onset of clinical symptoms. In 26 patients (11 children from 1 day to 6 year old and 15 adults from 17 to 70 year old) with central nervous system disorders (15 meningo-encephalitis, 5 meningitis, 1 myelitis, 1 polyradiculoneuritis, 1 **dementia**, 1 epilepsy and 2 other), alpha IFN is quantified using a cytopathic effect inhibition assay of VSV on MDBK cells. The mean value of alpha IFN is 80 UI/ml (range from 0 to 512 UI/ml). Virus involved are herpes virus in 38.5% of cases (10/26) and 66% of viral meningoencephalitis (8/12), H.I.V. in 3 cases, VZV in 2 and measles virus in 1 case. Viral aetiology is suspected in six other patients. The results show the importance of early determination of alpha IFN (immediately after the first symptoms and on the first admission to the hospital) in sera and cerebrospinal fluids (CSF) simultaneously with viral culture and antibody research. The presence of alpha IFN only in CSF and a higher titre of alpha IFN in CSF than in serum are important data to distinguish primitive acute necrotizing encephalitis from post eruptive or post infectious perivenous encephalitis. In herpes virus infections with specific **treatment** all the patients recover. However to prevent brain damage in survivors the **treatment** should be established as soon as possible.

L9 ANSWER 5 OF 14 MEDLINE
AN 92330969 MEDLINE
DN 92330969 PubMed ID: 1628224
TI **Treatment** of advanced colorectal cancer with recombinant **interferon** alpha and fluorouracil: activity in liver metastasis.
CM Comment in: Cancer Invest. 1994;12(1):101-4
AU Diaz Rubio E; Jimeno J; Camps C; Aranda E; Massuti B; Blanco E; Anton A; Lizon J; Gonzalez Larriba J L
CS Department of Medical Oncology, Hospital Clinico Universitario, Madrid, Spain.
SO CANCER INVESTIGATION, **(1992)** 10 (4) 259-64.
Journal code: 8307154. ISSN: 0735-7907.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199208

patients with mild symptomatic disease. Although one study has shown zidovudine to have no significant beneficial effects on survival or disease progression in patients with asymptomatic HIV infection, several other studies have shown zidovudine to delay disease progression in this patient group. Results from related ongoing studies are awaited with interest. Zidovudine reduces the incidence of AIDS **dementia** complex (ADC) and appears to prolong survival in these patients, and improves other neurological complications of HIV infection. The drug also appears to enhance the efficacy of **interferon**-alpha in patients with Kaposi's sarcoma. Although zidovudine is widely used as postexposure prophylaxis following accidental exposure to HIV, its efficacy in preventing seroconversion is unclear. Whether zidovudine prevents vertical transmission also remains to be determined. The overall efficacy of zidovudine in the **treatment** of children with HIV infection appears similar to that in adults despite more rapid disease progression in younger patients. Zidovudine-resistant isolates can emerge as early as after 2 months' therapy, and primary infection with zidovudine-resistant strains has been documented. Both zidovudine resistance and the syncytium-inducing HIV phenotype appear to be associated with poor clinical outcome. However, zidovudine resistance may revert on drug withdrawal or switching to an alternative therapy. Zidovudine-associated haematotoxicity may be dose-limiting. Nonhaematological adverse events associated with zidovudine therapy are generally mild and usually resolve spontaneously. Dosages of approximately 500 to 600 mg/day appear to be at least as effective as dosages of 1200 to 1500 mg/day and are better tolerated in patients with less advanced disease. However, optimal dosage are unclear. Despite beneficial effects, zidovudine monotherapy is not curative. There is evidence to suggest that the concomitant administration of zidovudine with didanosine or zalcitabine is effective in patients with HIV disease progression despite receiving zidovudine monotherapy, and there is some evidence that concomitant zidovudine plus didanosine therapy is more effective than alternating monotherapy. However, results from studies of combination therapy in asymptomatic patients, and from comparative combination therapy studies are awaited. Cotherapy with agents that augment haematopoiesis allows the continuation of therapeutic zidovudine dosages.(ABSTRACT TRUNCATED AT 400 WORDS)

L9 ANSWER 3 OF 14 MEDLINE
AN 93140257 MEDLINE
DN 93140257 PubMed ID: 1487856
TI An autopsied case of **interferon** encephalopathy.
AU Mitsuyama Y; Hashiguchi H; Murayama T; Koono M; Nishi S
CS Department of Psychiatry, Miyazaki Medical College, Japan.
SO JAPANESE JOURNAL OF PSYCHIATRY AND NEUROLOGY, **(1992 Sep)** 46 (3) 741-8.
Journal code: 8610886. ISSN: 0912-2036.
CY Japan
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199302
ED Entered STN: 19930312
Last Updated on STN: 20000303
Entered Medline: 19930222
AB A 78-year-old male with renal carcinoma was **treated** with a high dose infusion of **interferon**-alpha (IFN-alpha) for eight months. The patient had evidence of organic brain syndrome such as dysfunction of memory, slowing of behavior, and development of mental confusion that appeared eight months after the **treatment**. MRI at the time of mental confusion revealed diffuse white matter lesions. Neuropathologic findings were compatible to Binswanger's disease and Senile **Dementia** of Alzheimer Type (SDAT), Preexisting neurologic

L9 ANSWER 1 OF 14 MEDLINE
AN 95089191 MEDLINE
DN 95089191 PubMed ID: 7996704
TI Therapy for HAM/TSP and AIDS.
AU Nakagawa M; Maruyama Y; Osame M
CS Third Department of Internal Medicine, Faculty of Medicine, Kagoshima University.
SO NIPPON RINSHO. JAPANESE JOURNAL OF CLINICAL MEDICINE, **(1994 Nov)** 52 (11) 3019-25. Ref: 25
Journal code: 0420546. ISSN: 0047-1852.
CY Japan
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA Japanese
FS Priority Journals; AIDS
EM 199501
ED Entered STN: 19950126
Last Updated on STN: 19970203
Entered Medline: 19950113
AB (1) We evaluated efficacy of several **treatments** for HTLV-I-associated myelopathy (HAM) on the basis of our study on 254 HAM patients and of literature review. Improvement of motor disability more than fair response was obtained as follows: 82% in prednisolone, 69% in **interferon**-alpha, 92% in fosfomycin, 82% in high-dose vitamin C, 72% in blood purification therapy, 70% in heparin, 59% in salazosulfapyridine, 56% in thyrotropin-releasing hormone, 55% in erythromycin, 50% in mizoribine. (2) In the absence of clear guideline, the efficacy of zidovudine in the AIDS **dementia** complex has been demonstrated. There are also efficacy of amytriptylinein controlling HIV headache, corticosteroid in mononeuritis multiple and inflammatory myositis, hydrocortisone in autonomic neuropathy and plasmapheresis in distal sensory neuropathy respectively. Otherwise, it is emphasized that ddI, ddC and d4T have peripheral neuropathy as major, dose related side effect.

L9 ANSWER 2 OF 14 MEDLINE
AN 94038723 MEDLINE
DN 94038723 PubMed ID: 7693435
TI Zidovudine. An update of its pharmacodynamic and pharmacokinetic properties, and therapeutic efficacy.
AU Wilde M I; Langtry H D
CS Adis International Limited, Auckland, New Zealand.
SO DRUGS, **(1993 Sep)** 46 (3) 515-78. Ref: 450
Journal code: 7600076. ISSN: 0012-6667.
CY New Zealand
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LA English
FS Priority Journals; AIDS
EM 199312
ED Entered STN: 19940117
Last Updated on STN: 19970203
Entered Medline: 19931221
AB Zidovudine remains the mainstay in the **treatment** of patients infected with human immunodeficiency virus (HIV). The drug delays disease progression to acquired immunodeficiency syndrome (AIDS) and to AIDS-related complex (ARC), reduces opportunistic infections, and increases survival in patients with advanced HIV infection. There is evidence to suggest that zidovudine also delays disease progression in

L15 ANSWER 32 OF 42 USPATFULL
AN 1999:39938 USPATFULL
TI Treatment of autoimmune diseases, including AIDS
IN Skurkovich, Boris, Pawtucket, RI, United States
Skurkovich, Simon V., Rockville, MD, United States
PA Advanced Biotherapy Concepts, Inc., Rockville, MD, United States (U.S. corporation)
PI US 5888511 19990330
AI US 1996-771831 19961223 (8)
RLI Continuation-in-part of Ser. No. US 1993-25408, filed on 26 Feb 1993, now patented, Pat. No. US 5626843
DT Utility
FS Granted
EXNAM Primary Examiner: Scheiner, Toni R.
LREP Panitch Schwarze Jacobs & Nadel, P.C.
CLMN Number of Claims: 14
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2042
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present disclosure concerns the treatment of a patient with autoimmune disease, including AIDS, by neutralizing, removing or inhibiting different types of interferons, tumor necrosis factor, HLA class II antigens, IgE, and other pathological factors and/or their receptors, as well as neutralizing, removing or inhibiting autoantibodies, including antibodies to target cells, CD4 cells and DNA. Treatment comprises administration of an autoimmune inhibitor, or extracorporeal exposure of the patient's fluid to an immunosorbent comprising an autoimmune inhibitor, followed by return of the treated fluid to the patient, or it comprises a combined therapy involving extracorporeal immunosorption in conjunction with the administration of an autoimmune inhibitor.

post pd.

L4 ANSWER 4 OF 32 MEDLINE
AN 1998427779 MEDLINE
DN 98427779 PubMed ID: 9756348
TI Anti-gamma **interferon** can prevent the premature death of **trisomy** 16 mouse cortical neurons in culture.
AU Hallam D M; Maroun L E
CS Department of Medical Microbiology and Immunology, Southern Illinois University School of Medicine, Springfield 62794-1220, USA.
SO NEUROSCIENCE LETTERS, (1998 Aug 7) 252 (1) 17-20.
Journal code: 7600130. ISSN: 0304-3940.
CY Ireland
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199811
ED Entered STN: 19990106
Last Updated on STN: 19990106
Entered Medline: 19981125
AB Previous reports have indicated that human **trisomy** 21 and mouse **trisomy** 16 neurons exhibit decreased viability in culture when compared to euploid control cultures and that trisomic cells are significantly more sensitive to the anti-cellular effects of the **interferons**. In the study reported here, cortical neurons from euploid and **trisomy** 16 mouse fetuses were treated with either anti-gamma-**interferon** or non-specific IgG and neuron morphology and viability measured photographically. The addition of anti-gamma-**interferon** IgG to the culture media had no effect on euploid neurons, but significantly increased **trisomy** neuron viability throughout the 5-day culture period. Assay of both DNA fragmentation and phosphatidylserine externalization suggested that the trisomic neurons were undergoing apoptosis at a significantly higher rate than their euploid counterparts and that this increase in apoptosis could be almost completely prevented by addition of either ligand purified monoclonal or ligand purified polyclonal anti-gamma-**interferon** IgG. Taken together, these data suggest that endogenous **interferon** plays an important role in the premature death of the **trisomy** neuron.

L4 ANSWER 5 OF 32 MEDLINE
AN 96388790 MEDLINE
DN 96388790 PubMed ID: 8796190
TI **Interferon** action and chromosome 21 **trisomy** (**Down** syndrome): 15 years later.
AU Maroun L E
CS Southern Illinois University, School of Medicine, Department of Medical Microbiology Immunology, Springfield 62794-9230, USA.
SO JOURNAL OF THEORETICAL BIOLOGY, (1996 Jul 7) 181 (1) 41-6.
Journal code: 0376342. ISSN: 0022-5193.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199610
ED Entered STN: 19961022
Last Updated on STN: 19961022
Entered Medline: 19961010
AB A hypothesis relating **interferon** action and the chromosome 21 **trisomy** genotype and phenotype was presented in this journal in 1980. Since that time a number of additional genes involved in **interferon** action have been mapped to the distal **Down** Syndrome region of chromosome 21 and a growing literature has documented highly relevant pleiotropic effects of **interferon** in the brain. Thus, **interferon** continues to provide a potential basis for the phenotypic anomalies seen in the **interferon** supersensitive **Down** Syndrome patient. Further, the hypothesis that ribosomal RNA gene "satellite association" induced by **interferon** action is involved in the induction of chromosome 21 misdistribution at meiosis, is supported by extension of the cyclic correlation of **Down** Syndrome prevalence and virus epidemics, first observed by Stoller & Collmann in Australia from 1942 to 1964, to incidence data gathered by the CDC in the U.S. from 1968 to 1992. In addition, data from spontaneous abortuses and gametes assembled from the literature argue for a uniquely high frequency of chromosome 21 hyperploidy which suggests that the genes present on chromosome 21 play a role in its frequent misdistribution at meiosis. Taken together, these observations provide continued support for the hypothesis presented in 1980 that **interferon** action could be involved in the induction of both the **trisomy** 21 genotype and its resultant phenotype.

L15 ANSWER 41 OF 42 USPATFULL
AN 93:50658 USPATFULL
TI Interferon-gamma receptor fragment and its production
IN Novick, Daniela, Rehovot, Israel
Rubinstein, Menachem, Givat Shmuel, Israel
PA Yeda Research and Development Co. Ltd., Rehovot, Israel (non-U.S. corporation)
PI US 5221789 19930622
AI US 1990-578826 19900907 (7)
PRAI IL 1989-91562 19890907
DT Utility
FS Granted
EXNAM Primary Examiner: Russel, Jeffrey E.
LREP Cooper, Iver P.
CLMN Number of Claims: 4
ECL Exemplary Claim: 1
DRWN 5 Drawing Figure(s); 3 Drawing Page(s)
LN.CNT 555
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Soluble human IFN-gamma receptor extracellular fragment and salts, functional derivatives, precursors and active fractions thereof are provided in substantially purified form. They are useful as pharmaceutically active substances for protecting against the deleterious effects of IFN-gamma, e.g. in autoimmune diseases.

L15 ANSWER 42 OF 42 USPATFULL
AN 90:7543 USPATFULL
TI Human gamma interferon-specific receptor protein, antibody against said protein, methods for obtaining said protein and said antibody and compositions containing said protein and antibody
IN Novick, Daniela, Rehovot, Israel
Orchansky, Patricia, Rehovot, Israel
Fischer, Dina, Rehovot, Israel
Rubinstein, Menachem, Givat Shmuel, Israel
PA Yeda Research and Development Co., Ltd., Rehovot, Israel (non-U.S. corporation)
PI US 4897264 19900130
AI US 1987-30640 19870327 (7)
PRAI IL 1986-78444 19860408
DT Utility
FS Granted
EXNAM Primary Examiner: Rosenberg, Peter D.
LREP Browdy & Neimark
CLMN Number of Claims: 22
ECL Exemplary Claim: 1
DRWN 6 Drawing Figure(s); 6 Drawing Page(s)
LN.CNT 501
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Analysis of [.sup.125 I]. interferon gamma cross-linked to its receptor on various human cells by SDS-PAGE revealed that there are at least three different types of human interferon gamma receptors. In WISH, HeLa, FS11 and the other tissue cells an Mr 90,000-105,000 receptor was found. In monocytes and in the myeloid cell line KG-1 an Mr 140,000 receptor was found while in Daudi lymphoblastoid cells an Mr 95,000-115,000 receptor was found.

The various receptors were isolated from these cells by extraction followed by affinity chromotography on an immobilized interferon gamma column. The resulting purified preparations retained their original affinity for interferon gamma and were used for immunizing mice and subsequent development of highly specific antibodies.

L15 ANSWER 38 OF 42 USPATFULL
AN 96:109073 USPATFULL
TI **Soluble interferon**-gamma **receptor** fragment
IN Novick, Daniela, Rehovot, Israel
Rubinstein, Menachem, Givat Shmuel, Israel
PA Yeda Research and Development, Co., Ltd., Rehovot, Israel (non-U.S. corporation)
PI US 5578707 19961126
AI US 1993-16992 19930212 (8)
RLI Division of Ser. No. US 1990-578826, filed on 7 Sep 1990, now patented, Pat. No. US 5221789
PRAI IL 1989-91562 19890907
DT Utility
FS Granted
EXNAM Primary Examiner: Fitzgerald, David L.
LREP Cooper, Iver P.
CLMN Number of Claims: 7
ECL Exemplary Claim: 1
DRWN 5 Drawing Figure(s); 3 Drawing Page(s)
LN.CNT 608
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Soluble human IFN-gamma receptor extracellular fragment and salts, functional derivatives, precursors and active fractions thereof are provided in substantially purified form. They are useful as pharmaceutically active substances for protecting against the deleterious effects of IFN-gamma, e.g. in autoimmune diseases.

L15 ANSWER 36 OF 42 USPATFULL
AN 97:56515 USPATFULL
TI **Soluble interferon** .alpha.-**receptor**, its preparation and use
IN Revel, Michel, Rehovot, Israel
Abramovich, Carolina, Yavne, Israel
Ratovitski, Edward, Gan Yavne, Israel
PA Yeda Research and Development Co, Ltd., Rehovot, Israel (non-U.S. corporation)
PI US 5643749 19970701
AI US 1994-328256 19941024 (8)
PRAI IL 1993-107378 19931024
DT Utility
FS Granted
EXNAM Primary Examiner: Walsh, Stephen; Assistant Examiner: Brown, Karen E.
LREP Browdy and Neimark
CLMN Number of Claims: 12
ECL Exemplary Claim: 1
DRWN 11 Drawing Figure(s); 10 Drawing Page(s)
LN.CNT 1084
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB New forms of interferon .alpha.-receptors are provided. They may be prepared recombinantly and may be used in diagnosis and therapy.

L15 ANSWER 33 OF 42 USPATFULL
AN 1998:124409 USPATFULL
TI Nucleic acid encoding interferon-.alpha./.beta. binding protein
IN Novick, Daniela, Rehovot, Israel
Cohen, Batya, Tel-Aviv, Israel
Rubinstein, Menachem, Givat Shmuel, Israel
PA Yeda Research and Development Co. Ltd., Rehovot, Israel (non-U.S. corporation)
PI US 5821078 19981013
AI US 1995-385191 19950207 (8)
RLI Continuation-in-part of Ser. No. US 1993-115741, filed on 3 Sep 1993, now abandoned
PRAI IL 1992-103052 19920903
IL 1993-106591 19930804
IL 1994-108584 19940207
DT Utility
FS Granted
EXNAM Primary Examiner: Teng, Sally P.
LREP Browdy and Neimark
CLMN Number of Claims: 23
ECL Exemplary Claim: 1
DRWN 15 Drawing Figure(s); 10 Drawing Page(s)
LN.CNT 2048
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Interferon .alpha./.beta. binding proteins are provided, which are capable of modulating the activity of interferon-.alpha. subtypes as well as interferon-.beta.. Cloning of DNA molecules encoding these proteins, expression in host cells and antibodies against the proteins are also provided.